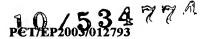
WO 2004/046175

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PCT/EP2003/012793

Figure 1, HCV J4L6 genome wild-type cDNA sequence, reference accession number AF054247,

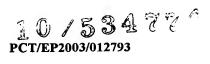
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9241	ctggctggtt	cgtcgctggt	tacagcgggg	gagacatata	tcacagcctg	tctcgtgccc
9301	gaccccgctg	gtttccgttg	tgcctactcc	tactttctgt	aggggtaggc	atttacctgc
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9421	ttttttt	tttttttt	tctttttt	tttctttcct	ttccttctt	ttttcctttc
9481	tttttccctt	ctttaatggt	ggctccatct	tagccctagt	cacggctagc	tgtgaaaggt
9541	ccgtgagccg	catgactgca	gagagtgctg	atactggcct	ctctgcagat	catgt

Figure 2, codon optimised HCV Core polynucleotide

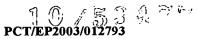


Figure 3, Codon optimised HCV NS3 polynucleotide

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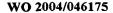
PCT/EP2003/012793

 ${\tt ATGGCGTGCATGTCCGCTGACCTGGAGGTGGTCACCTGA}$

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Figure 4, codon optimised HCV NS4B polynucleotide



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Figure 5, codon optimised HCV NS5B polynucleotide

ATGTCCATGTCCTACACCTGGACCGGCGCCCTGATCACCCCCTGCGCCGCCGAGGAGCAA GCTCCCGATTAACCCCCTGTCCAACTCTCTGCTCCGCCATCACAACATGGTGTATGCCACCA CCTCCCGCTCTGCGAGCCTCCGCCAGAAGAAGGTGACGTTCGACAGACTGCAGGTGCTGGAC GACCATTACAGGGACGTGCTGAAGGAAATGAAGGCCAAGGCTAGCACCGTGAAGGCCAAGCT GCTCAGCATTGAGGAGGCTTGCAAGCTGACCCCCCCCACAGTGCTAAATCCAAGTTCGGCT ACGGCGCCAAGGACGTGAGGAACCTGTCCTCGCGCGCTGTGAACCATATCCGCAGCGTGTGG GAGGACCTGCTCGAGGACACCGAGACCCCCATCGACAACCATCATGGCCAAGTCCGAGGT TGGGCGTGAGAGTCTGCGAGAAGATGGCCCTCTACGACGTGGTGTCCACCCTGCCGCAGGCC GTGATGGGGAGTTCCTACGGCTTCCAGTACAGCCCGAAGCAGAGGGTGGAGTTCCTGGTGAA CACGTGGAAGTCTAAGAAATGCCCCATGGGGTTCAGTTACGGAACAAGGTGCTTCGGGAGTA CTGTGACCGAATCCGATATCCGCGTGGAGGAGCATCTACCAGTGTTGTGACCTCGCCCCC GAGGCGAGACAGGCCATCCGCTCCCTGACCGAGAGGCTGTATATCGGCGGCCCACTGACCAA CAGCAAGGGGCAGAACTGCGGCTATCGCCGTTGTCGGGGCCTCCGGGGTGCTCACCACCTCTT GACTGCACCATGCTCGTGAACGGCGACGATCTGGTGGTGATCTGTGAGTCCGCGGGCACGCA GGAGGACGCGGCGCCTGCGGGCGTTCACAGAGGCCATGACACGCTACAGTGCCCCCCCG GCGACCCCCCCAGCCCGAATACGATCTGGAGCTCATCACTAGTTGCAGCTCGAACGTGTCT GTGGCCCATGACGCTTCTGGCAAACGGGTGTATTATCTGACGCGCGATCCCACCACCCCCCT CGCCAGAGCCGCGTGGGAGACAGCTCGGCACACCCCTGTGAACTCTTGGCTGGGCAACATCA TCATGTACGCCCTACCCTGTGGGCTCGCATGATCCTGATGACCCACTTCTTCAGTATCCTC CTCGCTCAGGAGCAGCTGGAGAAGGCGCTCGACTGCCAGATCTACGGCGCCTGCTATAGTAT ATAGTTACTCTCCTGGAGAAATTAACCGGGTGGCGAGCTGTCTGCGGAAGCTCGGCGTCCCC CCTCTGCGCGTTTGGCGCATCGCGCCAGGAGTGTGAGGCCAAGCTGCTGAGCCAGGGCGG AAGGGCCGCCACCTGCGGCCGGTATCTCTTCAACTGGGCCGTGCGCACCAAGCTCAAGCTCA GGCGACATCTACCACTCCCTCAGCAGGGCGCCCCCGCTGGTTCCCCCTGTGCCTGCT CCTGAGCGTCGGAGTCGGCATCTACCTGCTGCCCAACCGCTGA

Figure 6, Translation of HCV J4L6 genome (wild-type sequence)

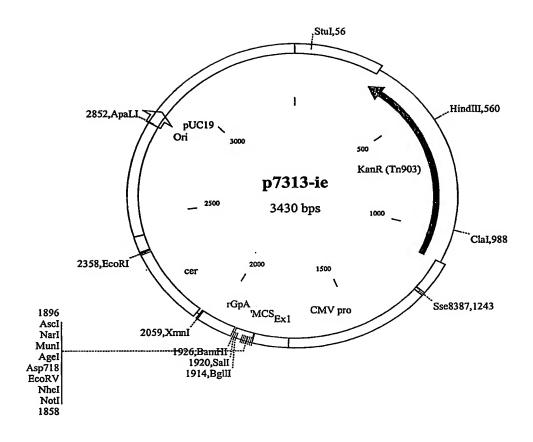
1 MSTNPKPQRK '	TKRNTNRRPQ 1	OVKFPGGGQI	VGGVYLLPRR (GPRLGVRATR I	KASERSQPRG
61 RRQPIPKARR	PEGRAWAQPG	YPWPLYGNEG	LGWAGWLLSP	RGSRPSWGPT	DPRRRSRNLG
121 KVIDTLTCGF	ADLMGYIPLV	GAPLGGAARA	LAHGVRVLED	GVNYATGNLP	GCSFSIFLLA
181 LLSCLTIPAS	AYEVRNVSGI	YHVTNDCSNS	SIVYEAADVI	MHTPGCVPCV	QEGNSSRCWV
241 ALTPTLAARN	ASVPTTTIRR	HVDLLVGTAA	FCSAMYVGDL	CGSIFLVSQL	FTFSPRRHET
301 VQDCNCSIYP	GHVSGHRMAW	DMMMNWSPTT	ALVVSQLLRI	PQAVVDMVAG	AHWGVLAGLA
361 YYSMVGNWAK	VLIVALLFAG	VDGETHTTGR	VAGHTTSGFT	SLFSSGASQK	IQLVNTNGSW
421 HINRTALNCN	DSLQTGFFAA	LFYAHKFNSS	GCPERMASCR	PIDWFAQGWG	PITYTKPNSS
481 DQRPYCWHYA	PRPCGVVPAS	QVCGPVYCFT	PSPVVVGTTD	RSGVPTYSWG	ENETDVMLLN
541 NTRPPQGNWF	GCTWMNSTGF	TKTCGGPPCN	IGGVGNRTLI	CPTDCFRKHP	EATYTKCGSG
601 PWLTPRCLVD	YPYRLWHYPC	TLNFSIFKVR	MYVGGVEHRL	NAACNWTRGE	RCNLEDRDRS
661 ELSPLLLSTT	EWQILPCAFT	TLPALSTGLI	HLHQNIVDVQ	YLYGVGSAFV	SFAIKWEYIL
721 LLFLLLADAR	VCACLWMMLL	IAQAEAALEN	LVVLNAASVA	GAHGILSFLV	FFCAAWYIKG
781 RLAPGAAYAF	YGVWPLLLLL	LALPPRAYAL	DREMAASCGG	AVLVGLVFLT	LSPYYKVFLT
841 RLIWWLQYFI	TRAEAHMQVW	VPPLNVRGGR	DAILLTCAV	HPELIFDITK	LLLAILGPLM
901 VLQAGITRVP	YFVRAQGLIR	ACMLVRKVAG	GHYVQMVFMK	LGALTGTYVY	NHLTPLRDWA
961 HAGLRDLAVA	VEPVVFSAME	TKVITWGADT	AACGDIILGL	PVSARRGKEI	FLGPADSLEG
1021 QGWRLLAPIT	AYSQQTRGVL	GCIITSLTGR	DKNQVEGEVQ	VVSTATQSFL	ATCINGVCWT
1081 VYHGAGSKTL	AGPKGPITQM	YTNVDLDLVG	WQAPPGARSM	TPCSCGSSDL	YLVTRHADVI
1141 PVRRRGDSRG	SLLSPRPVSY	LKGSSGGPLL	CPSGHVVGVF	RAAVCTRGVA	KAVDFIPVES
1201 METTMRSPVF	TDNSTPPAVP	QTFQVAHLHA	PTGSGKSTKV	PAAYAAQGYK	VLVLNPSVAA
1261 TLGFGAYMSK	AHGIDPNIRT	GVRTITTGGS	ITYSTYGKFL	ADGGCSGGAY	DILICDECHS.
1321 TDSTTILGIG	TVLDQAETAG	ARLVVLATAT	PPGSVTVPHP	NIEEIGLSNN	GEIPFYGKAI
1381 PIEAIKGGRH	LIFCHSKKKC	DELAAKLTGL	GLNAVAYYRG	LDVSVIPPIG	LAGTAVVVD
1441 MTGFTGDFDS	VIDCNTCVTQ	TVDFSLDPTF	TIETTTVPQD	AVSRSQRRGR	TGRGRSGIYR
1501 FVTPGERPSG	MFDSSVLCEC	YDAGCAWYEL	TPAETSVRLR	AYLNTPGLPV	CODHLEFWES
1561 VFTGLTHIDA	HFLSQTKQAG	DNFPYLVAYQ	ATVCARAQAP	PPSWDQMWKC	LIRLKPTLHG
1621 PTPLLYRLGA	VQNEVILTHP	ITKYIMACMS	ADLEVVTSTW	VLVGGVLAAL	AAYCLTTGSV
1681 VIVGRIILSG	KPAVVPDREV	LYQEFDEMEE	CASQLPYIEQ	GMQLAEQFKQ	KALGLLQTAT
1741 KQAEAAAPVV	ESKWRALETF	WAKHMWNFIS	GIQYLAGLST	LPGNPAIASL	MAFTASITSP
1801 LTTQNTLLFN	ILGGWVAAQL	APPSAASAFV	GAGIAGAAVG	SIGLGKVLVD	ILAGYGAGVA
1861 GALVAFKVMS	GEVPSTEDLV	NLLPAILSPG	ALVVGVVCAA	ILRRHVGPGE	GAVQWMNRLI
1921 AFASRGNHVS	PTHYVPESDA	AARVTQILSS	LTITQLLKRL	HQWINEDCST	PCSGSWLRDV
1981 WDWICTVLTD	FKTWLQSKLL	PRLPGVPFLS	CQRGYKGVWR	GDGIMQTTCP	CGAQIAGHVK
2041 NGSMRIVGPR	TCSNTWHGTF	PINAYTTGPC	TPSPAPNYSR	ALWRVAAEEY	VEVTRVGDFH
2101 YVTGMTTDNV	KCPCQVPAPE	FFTEVDGVRL	HRYAPACKPL	LREDVTFQVG	LNQYLVGSQL

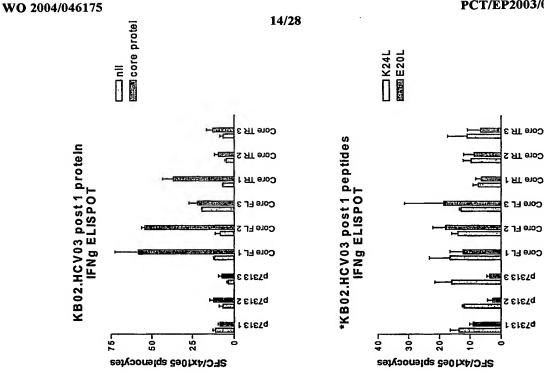
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2281	FPSALPIWAR	PDYNPPLLES	MKDbDAAbba	VHGCPLPPTK	APPIPPPRRK	RTVVLTESNV
2341	SSALAELATK	TFGSSGSSAV	DSGTATALPD	LASDDGDKGS	DVESYSSMPP	LEGEPGDPDL
2401	SDGSWSTVSE	EASEDVVCCS	MSYTWTGALI	TPCAAEESKL	PINPLSNSLL	RHHNMVYATT
2461	SRSASLRQKK	${\tt VTFDRLQVLD}$	DHYRDVLKEM	KAKASTVKAK	LLSIEEACKL	TPPHSAKSKF
2521	GYGAKDVRNL	SSRAVNHIRS	VWEDLLEDTE	TPIDTTIMAK	SEVFCVQPEK	GGRKPARLIV
2581	FPDLGVRVCE	KMALYDVVST	LPQAVMGSSY	GFQYSPKQRV	EFLVNTWKSK	KCPMGFSYDT
2641	RCFDSTVTES	DIRVEESIYQ	CCDLAPEARQ	AIRSLTERLY	IGGPLTNSKG	QNCGYRRCRA
2701	${\tt SGVLTTSCGN}$	TLTCYLKATA	ACRAAKLQDC	TMLVNGDDLV	VICESAGTQE	DAAALRAFTE
2761	AMTRYSAPPG	DPPQPEYDLE	LITSCSSNVS	VAHDASGKRV	${\tt YYLTRDPTTP}$	LARAAWETAR
2821	HTPINSWLGN	IIMYAPTLWA	RMILMTHFFS	ILLAQEQLEK	ALDCQIYGAC	YSIEPLDLPQ
2881	IIERLHGLSA	FTLHSYSPGE	INRVASCLRK	LGVPPLRTWR	HRARSVRAKL	LSQGGRAATC
2941	GRYLFNWAVR	TKLKLTPIPA	ASQLDLSGWF	VAGYSGGDIY	HSLSRARPRW	FPLCLLLLSV
3001	GVGIYLLPNR					

Figure 7, p7313-ie





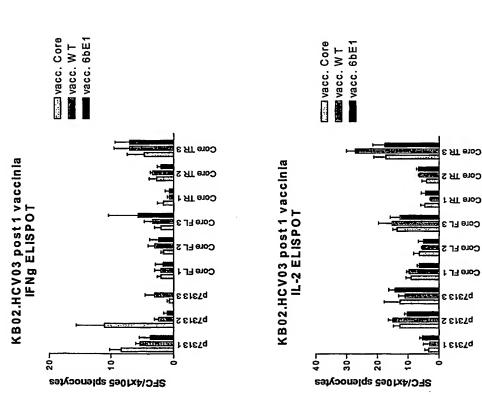
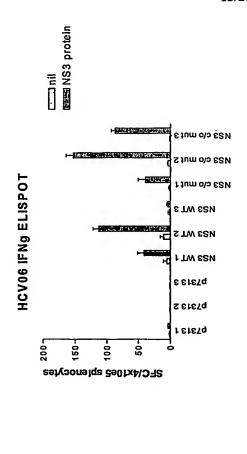
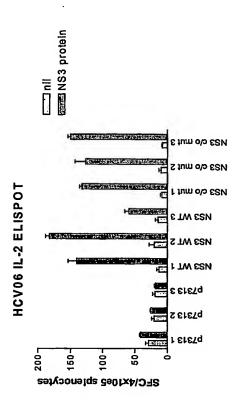
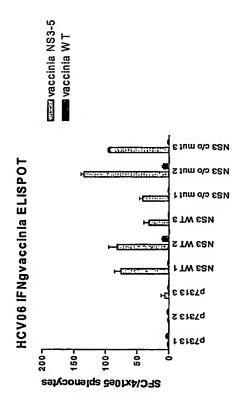


Figure 8, Immune responses to Core







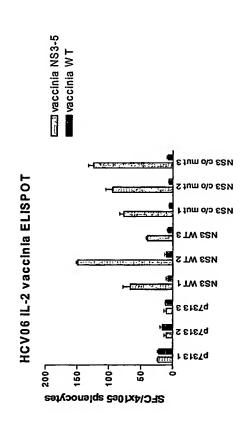
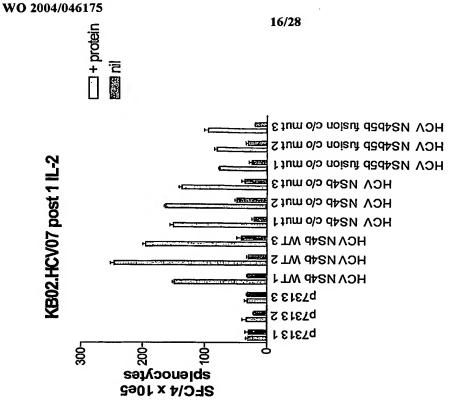


Figure 9, NS3 immunogenicity





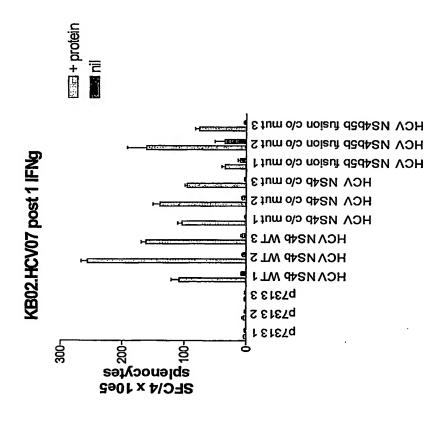
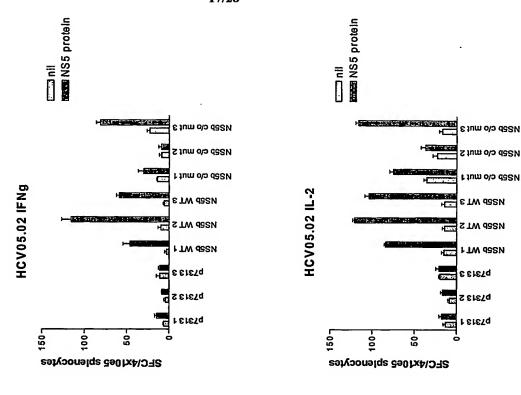
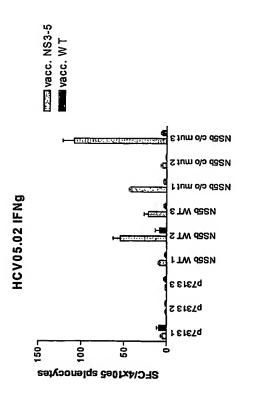


Figure 10, Immune responses to NS4B







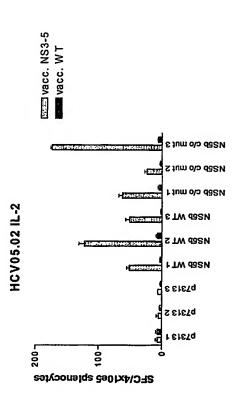


Figure 11, NS5B immune responses

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FIG. 12

Anti-HCV NS5B

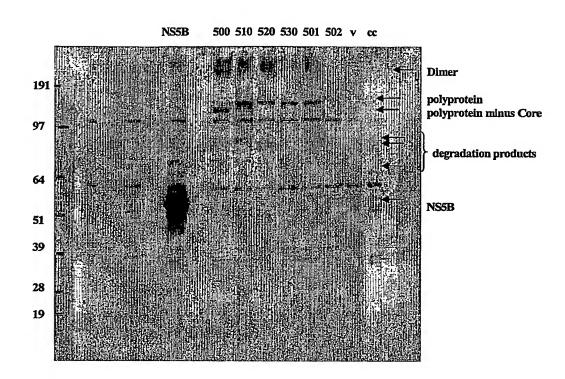
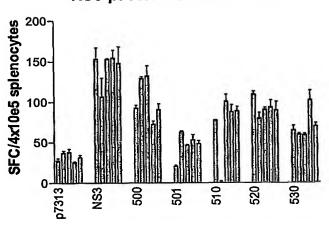


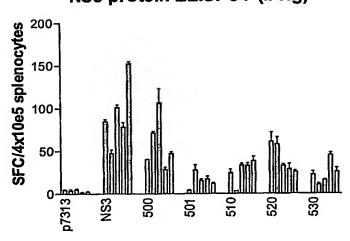
FIG. 13, A

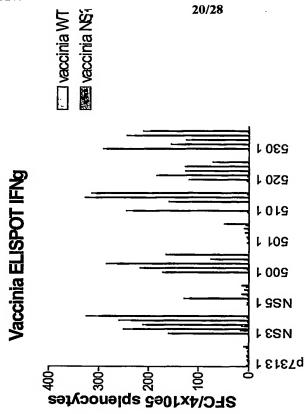
NS3 protein ELISPOT IL-2



в.

NS3 protein ELISPOT (IFNg)





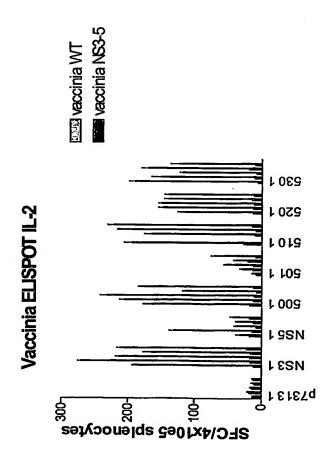
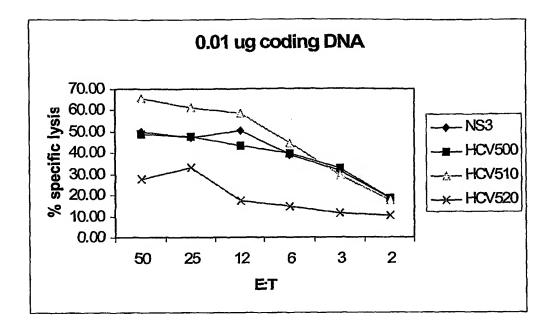


FIG 14.

FIG. 15,



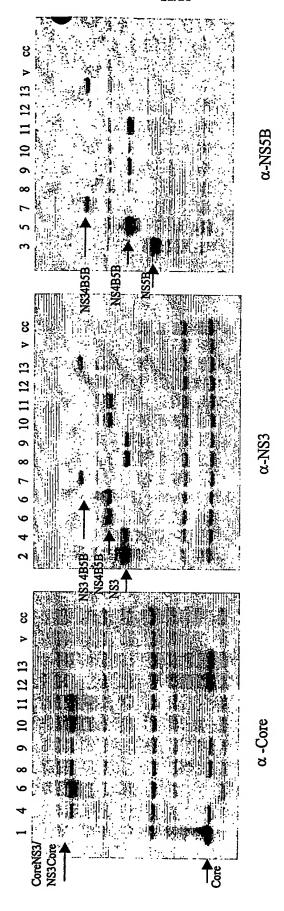


FIG. 16,

FIG. 17, Comparison of NS3 T cell response induced by dual promoter constructs.

KB03.HCV07 post primary IL-2 ELISpot

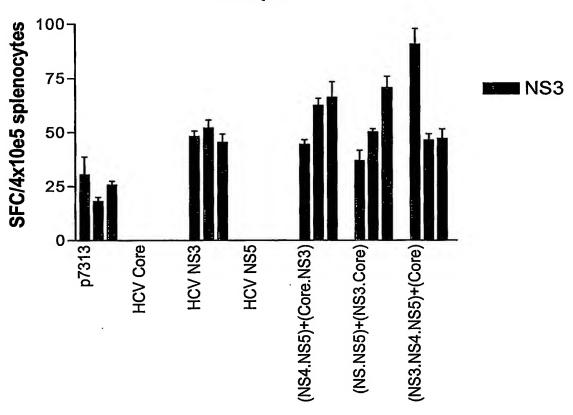
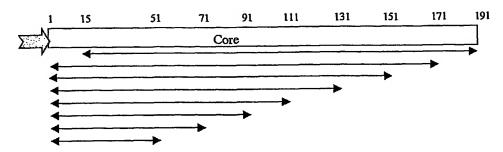


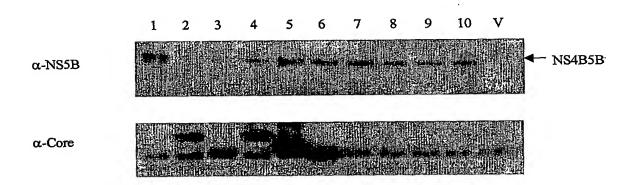
FIG. 18,



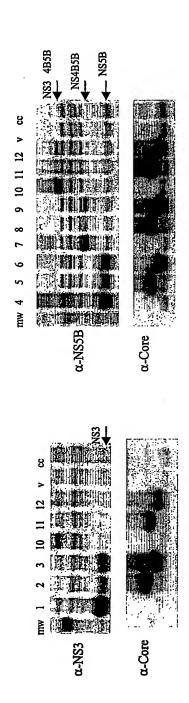
MW C191 CΔ15 C171 C151 C131 C111 C91 C71 C51



FIG. 19.



Effect of Core and Core, upon expression of NS3, NS5B, NS4B5B, and NS34B5B after co-transfection in 293T cells



Samples:

1. p7/NS3 + v

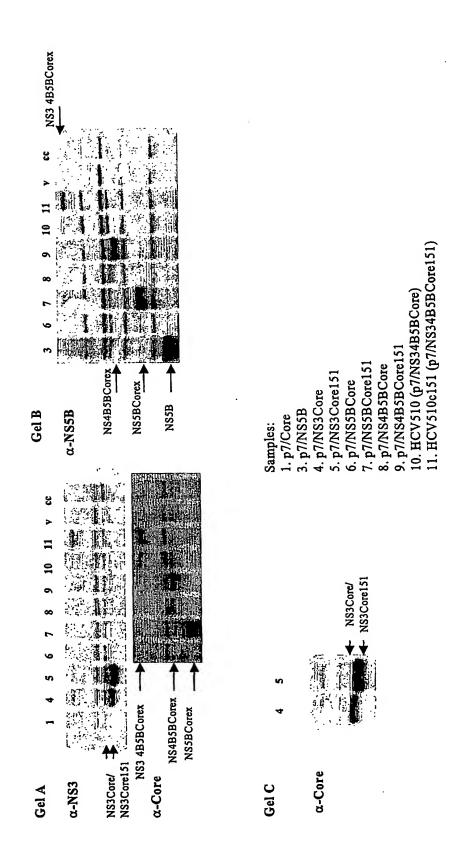
2. p7/NS3 + p7/Core
3. p7/NS3 + p7/Core151
4. p7/NS5B + v
5. p7/NS5B + v
5. p7/NS5B + p7/Core
11. p7/NS34B5B + p7/Core
6. p7/NS5B + p7/Core
12. p7/NS34B5B + p7/Core

FIG. 20,

PCT/EP2003/012793

Effect on expression of fusion proteins, after substitution of Coff, for Core₁₉₁, in transient transfection in 293T cells

FIG. 21,



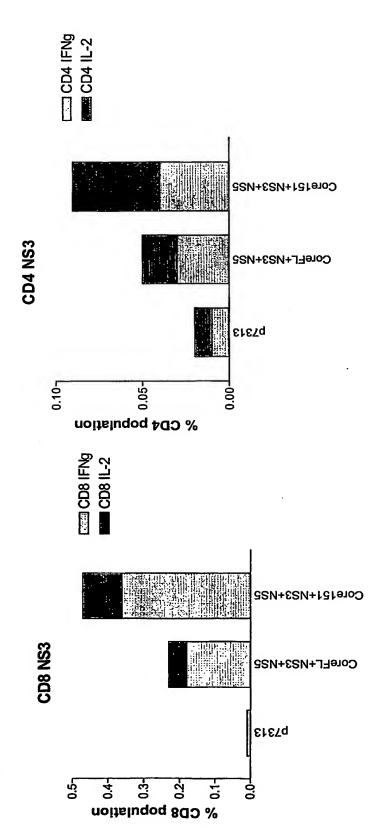
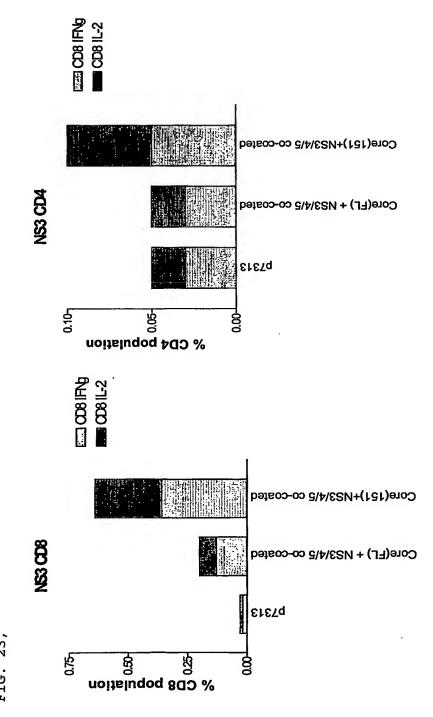


FIG. 22.



CC D1

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